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09/995,493	11/28/2001	Martin Handfield	01-662	1452

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1645	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No. 09/995,493	Applicant(s) HANDFIELD ET AL.	
	Examiner Padmavathi v Baskar	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1-14 and 17-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-28* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The preliminary amendment filed on 4/29/03 (Paper # 8), the response to restriction requirement filed on 4/29/03 (Paper # 9) and amendment filed on 5/28/03 (Paper # 11) has been entered into the record. New claim 28 has been added. Claims 1-5 have been amended. Claims 1-28 are pending in the application.

Drawings

2. No Drawings have been submitted in this application.

Information Disclosure Statement

3. The information disclosure statement (Paper # 5) is acknowledged and a signed copy of the same is enclosed here with this office action.

Restriction

4. Applicant's election with traverse of Group V, claims 15-16, SEQ.ID.NO: 52 in Paper # 9 (4/29/03) is acknowledged. Applicant requests the examiner that the newly added claim 28 is drawn to a method of detecting A.actinomycetemcomitans antibody in a test sample should be included along with the claims 15-16. The examiner added claim 28 to group V and will examine claims 15-16 and 28 with respect to SEQ.ID.NO: 52 in this application as the invention is drawn to a method of detecting A.actinomycetemcomitans antibody or antigen in a test sample. Therefore, claims 15-16 and 28 are under examination.

With respect to the sequences, applicant requests the examiner to modify the restriction requirement for sequences and prosecute the claims of group V with respect to polypeptides comprising at least five contiguous amino acids of SEQ.ID.NO: 226, 228, 230, 232 or 234. In addition, applicant also requests the examiner to examine polypeptides comprising at least five contiguous amino acids of SEQ.ID.NO: 2, 4 and 6 because more than one peptide comprising at least five contiguous amino acids of SEQ.ID.NO: 2, 4, 6, 226, 228, 230, 232 or 234 could be

practiced in diagnostic methods. Applicants, therefore, contend that in the context of the claims of Group V, polypeptides comprising at least five contiguous amino acids of SEQ.ID.NO: 2, 4, 6, 226, 228, 230, 232 or 234 would not possess different modes of operation, different functions or different effects.

The examiner's restriction under 35 USC 121 to one of the SEQ.ID.NO is based on the fact that all these sequences SEQ.ID.NO: 2 (185 amino acids), 4 (191 amino acids) 6 (266 amino acids), 226 (122 amino acids), 228 (155 amino acids), 230 (336 amino acids), 232 (246 amino acids) or 234 (142 amino acids) have different structures and therefore, have different functions and effects. The examiner did not restrict the sequences based on the polypeptide fragments. Further, there is nothing on this record to show them (at least five contiguous amino acids of SEQ.ID.NO: 2, 4, 6, 226, 228, 230, 232 or 234) to be obvious variants. Should applicants traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention(s).

5. Applicant is advised to amend the claims to read on SEQ.ID.NO: 52 only as it is an elected SEQ.ID.NO. Claims 15 and 28 are objected as they depend from non-elected claimed invention, said election made in Paper # 9.

6. Claims 1-14 and 17-27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected group.

Claim Rejections - 35 USC § 112, first paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 15-16 and 28 are rejected under 35 U.S.C. 112, first paragraph as containing subject mater which was not described in the specification in such a way so as to enable one skilled in the art to which it pertains or with which it is most nearly connected to make and/or use the invention.

Claims 15 and 16 are drawn to a method of detecting the presence of A.actinomycetemcomitans (Aa) or A.actinimycetemcomitans antigen (Aa antigen) in a test sample comprising: contacting a test sample with an antibody to an isolated polypeptide comprising at least 5 contiguous amino acids of SEQ.ID.NO: 52 that specifically binds to A.actinimycetemcomitans or A.actinimycetemcomitans antigen under conditions that allow formation of an immunocomplex between the antibody and the antigen; and detecting the immunocomplex, wherein detection of the immunocomplex indicates the presence of A.actinimycetemcomitans or A.actinimycetemcomitans antigen in a test sample, wherein A.actinimycetemcomitans antigen is expressed *in vivo* during infection of an animal.

Claim 28 is drawn to a method of detecting the presence of A. actinomycetemcomitans antibody in a test sample comprising: contacting a test sample with an isolated polypeptide comprising of at least 5 contiguous amino acids of SEQ.ID.NO: 52 that specifically binds to an antibody under conditions that allow formation or an immunocomplex between the antibody and the antigen; and detecting the immunocomplex, where in detection of the immunocomplex indicates the presence of A. actinomycetemcomitans antibody in a test sample.

The instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in In re Wands, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is drawn to methods of detecting the presence of Aa or Aa antigen in a test sample using an antibody that binds specifically to an isolated polypeptide comprising at least five contiguous amino acids of SEQ.ID.NO: 52, obtained from *in vivo* induced antigen technology (IVIAT), A.actinimycetemcomitans antigen is expressed *in vivo* during infection of an animal and a method of detecting the presence of Aa antibody using an antigen comprising at least 5 contiguous amino acids of SEQ.ID.NO: 52.

The state of the art in IVIAT technology indicates that it is possible that the product of an *in vivo* expressed gene obtained from this pioneering technology of in *vivo* expression system (IVES) will not be immunogenic (see page 337, right column, last paragraph in Trends in Microbiology 2000, 8; 337-339) although IVIAT avoids the use of animal models by using serum from patients who have experienced disease caused by the pathogen of interest. Further, it is not clear whether false positive reactions would occur due to immunological cross reactivity with (see page 337, right column, last paragraph in Trends in Microbiology 2000, 8; 337-339) other pathogens since it is an *in vivo* expressed antigen.

The specification teaches the polynucleotides and the polypeptides of the microbe Aa that are expressed *in vivo* using *in vivo* induced antigen technology (IVIAT). They are isolated and identified as SEQ.ID.NOS 1- 234. The specification also teaches polypeptide, SEQ.ID.NO:

52 containing 179 amino acids. However, the specification lacks support for any and all isolated polypeptide fragments comprising at least 5 contiguous amino acids of SEQ.ID.NO: 52 that are immunogenic. The specification lacks support for a method of detecting the presence of Aa or Aa antigen using an antibody that specifically binds to at least 5 contiguous amino acids of SEQ.ID.NO: 52 in a test sample obtained from an *in vivo* infected animal during infection. Further, it is not shown that these fragments would bind to serum from patients who have experienced disease caused by Aa that is crucial for this method to work.

The specification on page 2 teaches that A.actinomycetemcomitans (Aa), an etiologic agent of periodontal disease is not yet characterized. Further, the specification also indicates that no test so far has been developed to identify and differentiate between the presence of Aa in dental plaque (normal plaque) and the presence of Aa in dental disease process. In addition the claimed polypeptide, SEQ.ID.NO: 52 produced by IVIAT technology has not been characterized. It is not clear whether SEQ.ID.NO: 52 or its fragments are immunogenic and all serotypes of Aa during infection could be identified using either antibody that binds to at least 5 amino acids to SEQ.ID.NO: 52 or antigen comprising at least 5 amino acids of SEQ.ID.NO: 52 would bind to antibodies from infected individuals and thus the claimed method would be able to detect and differentiate all Aa strains in a test sample, obtained during infection. Further, there are no working examples to support specific antibodies that bind to Aa or to the claimed polypeptide fragments of SEQ.ID.NO: 52, which are important to differentiate Aa or Aa antigen present in plaque and in disease. The specification does not teach any antigen having five amino acids would be able to detect sera from infected individual. In view of the state of the art, the amount of guidance provided by the specification i.e., lack of working examples using five amino acids of SEQ.ID.NO: 52 and the nature of invention, a method of specifically detecting the presence of Aa or Aa antigen comprising at least 5 amino

acids of SEQ.ID.NO: 52 or antibody that binds to 5 amino acids of SEQ.ID.NO: 52 in a test sample is not sufficient to one skilled in the art to make and/or use the invention as claimed. Therefore, a method of specifically detecting the presence of Aa or Aa antigen comprising at least 5 amino acids of SEQ.ID.NO: 52 or antibody in a test sample obtained during infection must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

Claim Rejections - 35 USC 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claim 28 is rejected under 35 U.S.C. 102(b) as being anticipated by Flemmig et al 1996(Clinical and Diagnostic Laboratory Immunology; 3, 678-681).

The claim is drawn to a method of detecting the presence of *A. actinimycetemcomitans* antibody in a test sample comprising: contacting a test sample with an isolated polypeptide comprising of at least 5 contiguous amino acids of SEQ.ID.NO: 52 that specifically binds to an antibody under conditions that allow formation of an immunocomplex between the antibody and the antigen; and detecting the immunocomplex, where in detection of the immunocomplex indicates the presence of *A. actinomycetemcomitans* antibody in a test sample.

Flemmig et al disclose an immunoblotting method for detecting the presence of *A. actinomycetemcomitans* antibody (see abstract and page 679, left column under SDS-PAGE

and immunoblotting). The method comprises contacting membrane proteins from *A.* actinomycetemcomitans that were separated by gel-electrophoresis (SDS-PAGE) with sera from infected individuals and thus read on contacting a test sample with a polypeptide of the claimed invention. After washing, the strips were incubated with goat anti-human IgA or IgG or IgM conjugated with alkaline phosphatase. The presence of a band is considered positive because the antigen present on the strip bound to an antibody present in a test sample and forms an immunocomplex that is positively identified by goat anti-human IgA or IgG or IgM conjugated with alkaline phosphatase. The positive band indicates the presence of *A. actinomycetemcomitans* in a test sample (page 679, left column under SDS-PAGE and immunoblotting and figure 1). The disclosed outer membrane proteins inherently contain the claimed peptide comprising at least 5 contiguous amino acids of SEQ.ID.NO: 52 because the outer-membrane proteins were obtained from cell lysates that contain mixture of polypeptides including a peptide comprising at least 5 contiguous amino acids of SEQ.ID.NO: 52. Therefore, the prior art anticipates the claimed invention. In the absence of evidence to the contrary the disclosed prior art reads on the claimed invention since the OMP proteins bind to the specific anti-OMP antibodies. Characteristics such as including 5 contiguous amino acids of SEQ.ID.NO: 52 would be inherent in the preparations of OMP proteins. *See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.* . The prior art anticipates the claimed invention.

11. Claim 28 is rejected under 35 U.S.C. 102(b) as being anticipated by Ebersole et al 1995(J.Dent Res 74 (2) 658-666).

The claim has been discussed supra.

Ebersole et al disclose an immunoblotting method for detecting the presence of *A. actinomycetemcomitans* antibody (see abstract and page 659, right column under Western immunoblotting). The method comprises contacting outer membrane proteins from *A.* actinomycetemcomitans that were separated by gel-electrophoresis (figure1)) with sera from infected individuals and thus read on contacting a test sample with a polypeptide of the claimed invention. After washing the strips were incubated with goat anti-human IgA or IgG or IgM conjugated with alkaline phosphatase. The presence of a band is considered positive because the antigen present on the strip bound to antibody present in a test sample and forms an immunocomplex, which is positively identified by goat anti-human IgA or IgG or IgM conjugated with alkaline phosphatase. The positive band indicates the presence of *A. actinomycetemcomitans* in a test sample (page 660, left column under SDS-PAGE and immunoblotting and figure 2). The disclosed outer membrane proteins (OMP) contain the claimed peptide comprising at least SEQ.ID.NO: 52 because the outer-membrane proteins were obtained from cell lysates containing mixture of polypeptides including peptide comprising at least SEQ.ID.NO: 52. Therefore, the prior art anticipates the claimed invention. In the absence of evidence to the contrary the disclosed prior art reads on the claimed invention since the OMP proteins bind to the specific anti-OMP antibodies. Characteristics such as isolated polypeptide comprising at least 5 contiguous amino acids of SEQ.ID.NO: 52 would be inherent in the preparations of OMP proteins See *In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.* . The prior art anticipates the claimed invention.

12. Claims 15-16 are under 35 U.S.C. 102(b) as being anticipated by Snyder et al 1991 EPO 0439210 or EPO 0439211 or EPO0439212.

The claims are drawn to a method of detecting the presence of *A.actinimycetemcomitans or A.actinimycetemcomitans* antigen in a test sample comprising: contacting a test sample with an antibody to an isolated polypeptide comprising at least 5 amino acids of SEQ.ID.NO: 52 under conditions that allow formation of an immunocomplex between the antibody and the antigen; and detecting the immunocomplex, wherein detection of the immunocomplex indicates the presence of *A.actinimycetemcomitans or A.actinimycetemcomitans* antigen in a test sample, wherein *A.actinimycetemcomitans* antigen is expressed *in vivo* during infection of an animal.

Snyder et al 1991 EPO0439210, disclose an ELISA method for detecting the presence of Aa or Aa antigen by contacting the sample suspected of containing a microorganism Aa or antigen extract with polyclonal antibody conjugate, said antibody is specific to the Aa or Aa antigen (see page 2, lines 1-5, 51 through page 3, lines 1-15). They form an immunocomplex and said complex was detected with a label such as alkaline phosphatase or peroxidase etc (see example 1, page 9, line 51 through page 11, line 34), said Aa antigen is expressed during infection (se page 1, lines 57-64) causing periodontal disease and therefore the method detects the presence of Aa or Aa antigen in a test sample. The disclosed polyclonal antibody specifically binds to Aa peptide comprising at least 5 amino acids of SEQ.ID.NO: 52 since the polyclonal antibodies are raised against all Aa polypeptides. The prior art anticipates the claimed invention.

Or

13. Snyder et al, EPO 0439211 disclose an ELISA method for detecting the presence of Aa or Aa antigen by contacting the sample suspected of containing a microorganism Aa or extract of an antigen with polyclonal antibody conjugate, said antibody is specific to the Aa or Aa

antigen (see page 8, column 13 through column 14, line 8) and forms an immunocomplex and said complex is detected with a label such as alkaline phosphatase or peroxidase etc (see page 8 column 14, line 9 through page 9, column16, line 27), said Aa antigen is expressed during infection (se page 1, lines 57-64) causing periodontal disease and therefore the method detects the presence of Aa (as low as 3000cells) or Aa antigen in a test sample. The disclosed polyclonal antibody specifically binds to Aa peptide comprising at least 5 amino acids of SEQ.ID.NO: 52 since the polyclonal antibodies are raised against all Aa polypeptides. The prior art anticipates the claimed invention. Or

14. Snyder et al, EPO 0439212 disclose an ELISA method for detecting the presence of Aa or Aa antigen by contacting the sample suspected of containing a microorganism Aa or extract of an antigen with an polyclonal antibody conjugate, said antibody is specific to the Aa or Aa antigen and forms an immunocomplex and said complex is detected with a label such as alkaline phosphatase or peroxidase etc (see page 13, column 21 and page 14, column 23 through column 24, lines 31), said Aa antigen is expressed during infection (se page 1, left column lines 5 through right column) causing periodontal disease and therefore the method detects the presence of Aa or Aa antigen in a test sample. The disclosed polyclonal antibody specifically binds to Aa peptide comprising at least 5 amino acids of SEQ.ID.NO: 52 since the polyclonal antibodies are raised against all Aa polypeptides. The prior art anticipates the claimed invention.

15. Claims 15-16 are under 35 U.S.C. 102(b) as being anticipated Snyder et al 1992, EPO 537830.

The claims have been discussed supra.

Snyder et al 1992, disclose an ELISA method for detecting the presence of Aa or Aa antigen from different patients suffering from periodontal disease by contacting the antigen extract in a surfactant mixture with an antibody, specific to A.actinomycetemcomitans (see page 8, lines 17-45) in an ELISA plate. Immediately, peroxide/ antibody conjugate was added to the wells and sandwich complex formation was allowed for five minutes. After the last wash, the dye was added and the resulting signal was evaluated for the presence of Aa or Aa antigen in a test sample (see pages 8 - 9, lined 24-46 and Table 1, lines 5-15). The prior art anticipates the claimed invention.

Status of Claims

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

8/8/03

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